Leptin Receptors can be an Alternative Target for New Anti-hypertensive Drug Development

Sir,

It has been demonstrated by various researchers that leptin is a pleiotropic hormone and has multiple actions relevant to control of feeding, cardiovascular functions, insulin resistance, angiogenesis, immune response, and hematopoiesis.

The prime role is by regulating the adipose-tissue mass through hypothalamic control on hunger and energy use. It acts by binding with Leptin receptor also known as LEP-R or OB-R which takes pivotal role in the satiety signaling mechanism for food intake and energy metabolism.

Beginning with hypertension, Suter *et al*.[1] and Kennedy *et al*.[2] have demonstrated a relationship between elevated blood pressures and plasma leptin levels in hypertensive patients. Then, Makris *et al*.[3] demonstrated higher leptin and insulin levels in healthy offspring of hypertensive patients compared to healthy offspring of normotensive patients, which support the hypothesis that hyperleptinemia may contribute to hypertension.

Leptin causes high blood pressure: Though the clinical evidence for this view is still not very strong, however, leptin does indeed have peripheral physiological effects that suggest it may have a link in the triad of obesity, hyperinsulinemia, and hypertension.

Leptin, insulin concentrations and body weight are interrelated and there is a direct correlation between insulin and leptin levels. It is speculated that insulin and leptin interact and modulate each other's effects and contribute to hypertension through effects on renal tubular sodium handling.

Angiotensinogen (the substrate from which the hypertensive hormone angiotensin II (ANG II) is formed), is expressed in adipose tissue, and adipocytes have been shown to synthesize ANG II.[4] Hence in normotensive men AGT levels are related to both fat mass and plasma leptin levels, and there is a significant positive relationship between plasma leptin and plasma renin activity in hypertensive patients.

Chronic leptin infusion is shown to increase heart rate and blood pressure in animal models via stimulation of sympathetic nervous system activity.[5]

Hyperleptinemia predicts acute cardiovascular events, restenosis after coronary injury such as angioplasty and cerebral stroke independent of traditional risk factors, which is demonstrated by several clinical trials. Leptin-deficient hyperlipidemic mice develop significantly less atherosclerosis than mice on an atherogenic diet. Exogenous leptin significantly increases atherosclerotic areas in mice. In pathological conditions like obesity, the balance of leptin actions may shift to stimulate vascular inflammation, oxidative stress, and vascular smooth muscle hypertrophy.[2] These actions may contribute to the pathogenesis of hypertension, atherosclerosis, left ventricular hypertrophy, and type 2 diabetes mellitus. Also Insulin resistance systemic hypertension, and hypercholesterolemia all contribute independently to vascular endothelial dysfunction that promotes atherosclerosis and coronary heart disease. Taken together, these findings support the notion that leptin accelerates atherosclerosis and other cardiovascular complications. In conclusion, it was understood that irrespective of its direct action, leptin was found to be one among the etiologic cause behind the genesis of metabolic hypertension associated with hyperglycemia and hyperlipidemia.

Hence, developing a molecule which modulates the leptin receptors may be another potential target for alleviating

hypertension associated with metabolic deformity and hope can regulate the energy metabolism as well.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Quick Response Code:

Website: www.ijem.in

DOI: 10.4103/ijem.IJEM_564_17

How to cite this article: Ramkumar M, Kanthlal SK. Leptin receptors can be an alternative target for new anti-hypertensive drug development. Indian J Endocr Metab 2017;21:929-30.